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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/742,892	12/21/2000	Jack Gauldie	GDI-2	8232

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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/742,892	GAULDIE ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 October 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ they raise the issue of new matter (see Note below);
   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____.
3. ☐ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1,4-14,17-19 and 21-25*.

   Claim(s) withdrawn from consideration: _____.
8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

Continuation of 3. Applicant's reply has overcome the following rejection(s): The rejection of claims 1-24 under 35 USC 112, first and second paragraphs for new matter and indefiniteness.

Continuation of 5. does NOT place the application in condition for allowance because: The claims as amended lack enablement for the reasons of record. Claims 1-24 are directed to a vaccine "useful in treating diseases caused by P.acnes, and methods of treating said diseases. This intended use is considered to embrace a broad scope embracing reducing the size of abcesses caused by P.acnes infections to completely inhibiting or curing any disease caused by P.acnes, including acne vulgaris. The specification teaches a working example in an animal model in which a significant reduction in abcess size is measurent in mice that were injected i.m with an adenovira vector encoding P.acnes lipase prior to injection of P.acnes. The specification does not teach treatment of any disease other than acne, and does not teach a complete cure or total prevention. Applicant considers the enablement rejection at pages 11-19 of the response. A pages 12 and 13 of the response, Applicant considers the relevance of the McCluskie reference, cited by the Examiner to demonstrate th unpredictability in extrapolating the results in mouse DNA vaccine experiments to those that might be obtainedin humans. Applicant argues that McCluskie addresses only naked DNA vaccines, not virus-mediated immunization, and concludes that McCluskie cannot support the rejection. This is unpersuasive because claims 1, 7-14, 19, and 21-24 are not limited to a viral vector and clearly encompass naked DNA vaccines. Furthermore, Applicant has provided no evidence or reason to expect that the results in McCluskie would not hold true for virus mediated vaccines as well.

Applicant argues at pages 12 and 13 that the results of McCluskie are of questionable scientific value due to serious flaws in experimetal design. Applicant asserts that in mice disproportionately large dosage and injection volumes are used. Applicant notes that McCluskie indicates that the doses used in mice are proportionally greater than those used in humans to date. Applicant concludes that the results i McCluskie cannot substantiate the view that mouse immune responses to DNA vaccines do not predict similar results in humans. This is unpersuasive because Applicant has presented no data to indicate that proportionately greater doses have proven effective in other large experimental mammals. While McCluskie, in presenting a balanced view of the art, has provided a plausible explanation for the lack of ability to extrapolate mouse results to humans and larger primates, no evidence has been presented to indicate that this suggestion is correct, or that the art is of sufficient predictability to make such an extrapolation. McCluskie concludes that such extrapolations are not warranted.

Applicant argues at pages13-15 that others do not share the opinions expressed in McCluskie. For support Applicant relies upon the declaration nof Dr. Kumar which states that there have been 509 gene therapy trials since the 1980s. Applicant concludes that this is proof that those of skill in the art do not consider transfection and expression of vectors in human cells unpredictrable. This is unpersuasive because the issue of of enablement of the claims does not rest on whether or not one can transfect and express proteins in humans in vivo. Instead the issue is whether or not one can inhibit , prevent or cure diseases caused by P.acnes by delivery of nucleic acid molecules encoding P. acnes lipase. Applicant has presented no evidence that any one of these 509 trial has led to a a therapeutic result, and has presented no evidence that the state of the art is predictable with respect to extrapolating mouse results to humans.

At pages 15 and 16 Applicant argues that the routes of administration recited in the claims are enabled. For support Applicant relies upon McCluskie at pages 289-290, and Lewis et al (1999). This is unpersuasive because the passage indicated in McCluskie does not indciate that success was obtained by any of these routes, and the overall findings of McCluskie are as stated in the rejection, i.e. the route of administration "influences the strength and nature of immune responses in mice and non-human primates. However, the results in mice were not always predictive of those in monkeys and this is likely true for humans as well. Optimal dose and immunization schedule will most likely vary between species. It is not clear whether results in non-human primates will be predictive of results in humans, thus additional studies are required." McCluskie tested eight injection-mediated routes including intravenous, intramuscular, subcutaneous, and intraperitoneal, six non-injection routes including the claimed oral, ocular, inhalation, and intrarectal routes, and one transcutaneous route (gene gun). The results indicated that whereas substantial immune responses were obtained by IM, IV, sublingual, and intradermal injection, as well as by gene gun, none of the non-injection routes gave rise to any antibodies. See abstract, and Fig. 1 on page 291. This is objective evidence that the route of DNA delivery influences the immune response obtained in genetic immunization and that the results obtained by oral, ocular, inhalation, and intrarectal routes are unpredictable. Applicant has presented no evidence to the contrary. For example, Applicant has not pointed to any passsage in Lewis (1999) that provides any contraindication of the conclusions of McCluskie.

At pages 16 and 17, Applicant argues that the working example demonstrates that the claimed vaccine can treat P.acnes-related conditions. This is not at issue. The issues are whether or not these results can be extrapolated to humans, and whether or not the specification enables the breadth of the claims that includes complete inhibition and cure. Applicant has presented no evidence that the results can be extrapolated, i.e. that the model used is an accepted animal model, or that the differences between mouse and human physiology are insignificant in the context of the invention, and Applicant has presented no evidence that one of skill in the art would expect to be able to completely inhibit or cure any P.acnes-caused disease.

Applicant discusses to the written description rejection at pages 19-20 of the rejection.

The claims as amended are drawn to the genus of nucleic acids encoding a P.acnes lipase, or fragment thereof. The specification provides guidance as to how to obtain a lipase gene from P.acnes, but does not disclose the sequence of any lipase gene or polypeptide including the one used in the working example. Applicant asserts at page 20 of the response that the lipase gene obtained in the workin example is identical to that known in the prior art, but this assertion is unsupported by evidence. Applicant argues that because the prior art taught a sequence of a P.acnes lipase, one of skill in the art could readily learn that sequence. However, the claims are not drawn to a vaccine comprising any particular P.acnes lipase sequence, so they embrace any naturally existing, or recombinantly produced variant of a lipase derived from P.acnes. The specification as filed discloses none of these variants or their fragments. Given this disclosure, on of skill in the art could not conclude that Applicant was in possession of the claimed genus at the time the invention was filed

Applicant discusses to the anticipation rejection at pages 21 and 22 of the response. Applicant argues that the vaccine of Stickl does no comprise a vector as defined by the specification, specifically, the composition of Stickl does not comprise "genetically engineered nucleic acid constructs". This is unpersuasive because Applicant has not shown how the nucleic acid in the vector of Stickl differs from any genetically engineered construct. The nucleic acids in the vector of Stickl are the product of natural selection, and as such have been genetically engineered through mutation and recombination. For these reasons the rejection is maintained.

DAVE T. NGUYEN
PRIMARY EXAMINER